ADDITIONAL TECHNICAL PROPOSAL INSTRUCTIONS, FORMAT FOR TECHNICAL PROPOSAL, and TABLE OF CONTENTS

A SYSTEMS BIOLOGY APPROACH TO INFECTIOUS DISEASES RESEARCH
BAA NIH-NIAID-DMID-08-22

It is strongly recommended that offerors use the following template as the Table of Contents for the Technical Proposal. All information presented in the Technical Proposal should be presented in the order specified below.

These additional Technical Proposal instructions reflect the requirements of the BAA and provide specific instructions and formatting for the Technical Proposal. While Section L.2.b. of the BAA provides a generic set of Technical Proposal instructions applicable to all NIH R&D solicitations, these instructions are tailored to the specific requirements of the BAA. The information requested in these instructions should be used to format and prepare the Technical Proposal, and should be used as a Table of Contents for your Technical Proposal. Offerors should follow the instructions in Section L of the solicitation, and include the information requested here.

Offerors are advised to give careful consideration to the Broad Agency Announcement Description, Background and Introduction, Research and Technical Objectives, all reference materials, and attachments, the Technical Evaluation Criteria in Section M, and the BAA as a whole in the development of their Technical Proposals.

Offerors proposing subcontracts to perform portions of the Statement of Work should clearly identify the specific tasks for which they plan to utilize subcontractors, as well as the method and level of integration/coordination between the prime Contractor and all proposed subcontractors, and the expected advantages of such an approach.

Offerors are reminded that the total page limitation for the entire Technical Proposal is 175 pages including all appendices and attachments. Any pages in excess of this limit will be expunged from the proposal and will not be considered in the technical review. Proposals shall NOT include links to Internet Web site addresses (URLs) or otherwise direct readers to alternate sources of information.

TECHNICAL PROPOSAL – TABLE OF CONTENTS

SECTION 1:

This Section will precede the Technical Proposal requirements identified in Section L.2. of the BAA.

I. PROPOSAL TITLE PAGE. Include BAA title and number, name of organization, DUNS number, proposal part, and identify if the proposal is an original or a copy.

II. PROJECT OBJECTIVES, NIH FORM 1688
III. GOVERNMENT NOTICE FOR HANDLING PROPOSALS
IV. PROPOSAL SUMMARY AND DATA RECORD (NIH-2043)
V. TABLE OF CONTENTS

SECTION 2: TECHNICAL PROPOSAL OVERVIEW (suggested 3-page maximum)

Provide a brief overview of the proposed Systems Biology Program, including:

1) Scope of the Systems Biology Program and the approach that will be used to perform research in infectious diseases;
2) Systems biology Projects to be carried out by the offeror and the subcontractors, the targeted microbial organisms and the high-throughput technologies to be utilized;
3) Multidisciplinary nature of the research teams assembled for the Program and how the individuals in the team will cooperate;
4) Activities to be performed by the offeror and those that shall be provided by any proposed subcontractors;
5) Facilities, equipment and other resources to be made available by the offeror and any proposed subcontractors; and
6) Period of contract funding requested, a summary of the direct costs and total budget for each year.

SECTION 3: TECHNICAL PLAN/APPROACH

Offerors shall provide the following information as part of their Technical Proposal:

A. Systems Biology Program for Infectious Diseases Research

Describe the proposed large-scale, coordinated Systems Biology Program for Infectious Diseases Research to comprehensively and systematically analyze the molecular pathways, or other types of molecular interaction networks of microbial pathogens and/or their interaction with the host cells, using a combination of high-throughput "omics" experimental technologies and computational approaches. Include a detailed description of the following:

a. The proposed computational and experimental approaches to comprehensively and systematically analyze the molecular pathways (e.g., signaling, regulatory, metabolic), or other types of molecular interaction networks of microbial pathogens and/or their interaction with the host cells.

b. The Systems Biology Program research Projects proposed, their experimental design, and the rationale for using a combination of computational and experimental approaches. Describe how these two approaches will complement and inform each other to enhance the knowledge of the overall complexity of the biological, biochemical and biophysical molecular processes in microbial organisms and host cells, which may lead to the initiation and progression of infectious diseases. For each research Project proposed:

i. identify the specific aims;

ii. indicate the targeted organisms. If relevant, describe how they are phylogenetically related to the pathogens in the NIAID Category A-C priority lists for biodefense research (http://www3.niaid.nih.gov/biodefense/bandc_priority.htm) or why they may be considered as causing emerging/re-emerging infectious diseases;

iii. indicate the type of host cells that will be used, if appropriate. If studies are proposed that use cells of model host organisms for human infectious diseases instead of human cells, provide a description of how the research findings of the proposed projects are applicable and relevant to the study of infectious diseases in humans;

iv. explain how the research findings about functional molecular networks of the targeted organisms may potentially be applicable or relevant to a variety of pathogenic organisms, either within a species or across related species, based on knowledge retrieved from experimental studies, or through computational comparative genomic investigations;

v. describe the concurrent utilization of the informatics, functional genomics and proteomics cores at the initiation of contract support, and the utilization of at least one of the metabolomics, glycomics and lipidomics cores within the second year of the contract period;

vi. explain how the experimental data generated by the Program's high-throughput technology cores, as well as other data retrieved from publicly accessible genomic resources, such as those established by the NIAID-supported genomic research programs, will be analyzed, integrated and utilized to perform computational modeling in support of the systems biology studies of the pathogen or of its interaction with the host cells.

c. The breadth of expertise of the scientific and technical research teams of investigators and how effective communication and coordination among members of the multidisciplinary research teams will be achieved.

B. Offeror's Proposed Statement of Work (recommended 10 pages)

In contracts awarded under this BAA, the Statement of Work shall be the Statement of Work proposed by the offeror and negotiated and accepted by the NIAID. This section of the offeror's Technical Proposal should outline the activities to be performed by the Contractor during performance of the contract using an outline format. The offeror's proposed Statement of Work should begin as follows: "Independently, and not as an agent of the Government, the Contractor shall furnish all necessary services, qualified professional, technical, and administrative personnel, material, equipment and facilities, not otherwise provided by the Government under the terms of this contract, as needed to perform the tasks set forth below.

Specifically, the Contractor shall: ". The opening paragraph should be followed by a full Statement of Work describing each activity that the Contractor shall perform after the award of the contract. The Statement of Work shall include all activities required to effectively utilize a systems biology approach to comprehensively and systematically analyze molecular pathways (e.g., signaling, regulatory, metabolic) or other types of molecular interaction networks of microbial pathogens and/or their interaction with the host cells, using a combination of high-throughput experimental technologies and computational approaches. The Statement of Work should also include a description of all items to be delivered to the Government during performance of the contract, such as progress reports, financial reports, end products, and other deliverables and a timetable for their delivery.

The Statement of Work is distinguished from other sections of the Technical Plan in that the Statement of Work explicitly identifies what the Contractor shall provide. The other sections of the Technical Plan describe the specific detailed plans and approaches for establishing a large scale, coordinated Systems Biology Program.

Each activity described in the Statement of Work will begin with the words "The Contractor shall…" Where appropriate, divide the Statement of Work into separate Activities and Sub-activities. Examples of Activities and Sub-activities include:

- Activity: The Contractor shall provide the equipment, facilities and other resources required for systems biology analyses that use a combination of experimental and computational approaches to study molecular pathways of microbial pathogens and their interaction with the host. For each Systems Biology Program research Project:
  - Sub-activity: design and conduct experimental studies of regulatory and metabolic pathways in one specific microbial species in the NIAID Category A-C priority lists for biodefense research, their closely related species and their interaction with the host immune response genes;
  - Sub-activity: use informatics, functional genomics and proteomics cores (in year 1 and beyond) and a glycomics core (in year 2 and beyond) to identify the components and reactions of the molecular networks; and
  - Sub-activity: use an informatics core to analyze the data generated by the technology cores to develop a simulation model of the reaction networks.
- Activity: The Contractor shall disseminate contract-generated resources to the scientific community through:
  - Sub-activity: the development and maintenance of a public web portal; and
  - Sub-activity: the transfer of contract-generated data to a public repository.

NOTE: Please do not identify the offeror's name, Principal Investigator or other Key Personnel in the Statement of Work.

SECTION 4: PROVISION OF CONTRACT-GENERATED RESOURCES TO THE SCIENTIFIC COMMUNITY

A. Plan for the Public Release of Contract-Generated Resources: Describe the overall technical and administrative procedures and timelines that will govern the public release to the scientific community of the resources generated or improved during the performance of the contract, such as data, reagents, experimental protocols, software and algorithms.

B. Systems Biology Program Web Portal: Describe the methods for designing, implementing, and maintaining a public website that illustrates the Systems Biology Program, lists relevant publications, provides access or links to contract-generated resources, and captures web site access metrics.

SECTION 5: SCIENTIFIC AND TECHNICAL PERSONNEL

The Technical Proposal should include all information relevant to document individual training, education, experience, qualifications and expertise necessary for the successful completion of all contract requirements. Limit CVs to 3 page maximum and provide selected references for publications relevant to the scope of the BAA.

A. Principal Investigator (PI): Describe and document the experience and qualifications of the PI to plan, manage, and direct the scientific and administrative activities to be carried out under this contract. Provide the percentage of total time the PI will commit to the proposed Systems Biology Program. Describe previous experience with research projects having goals, size and complexity similar to those of the proposed Program (limit to the past 5 years). Report previous experience of the PI in leadership roles. Include details documenting the PI's experience in achieving milestones and deadlines; tracking, monitoring, and reporting project status and progress; and monitoring costs.

B. Project Manager (PM): Describe and document the experience and qualifications of the PM to monitor the activities to be carried out under this contract. Provide the percentage of total time the PM will commit to the proposed Systems Biology Program. Describe previous experience with projects having goals, size and complexity similar to those of the proposed Program (limit to the past 5 years). Report previous experience of the PM in project management and other leadership roles, in particular those for which fostering of communication and coordination across multidisciplinary teams of investigators or of subcontractors was necessary. Include details documenting the PM's experience in tracking, monitoring, and reporting Program and research Projects status and progress, and monitoring the budget.

B. **Other Key Scientific and Technical Personnel:** Describe the training, education, experience, qualifications and documented capability of the senior scientific and technical personnel for the proposed research Program, each Project, and each Core. Provide the percentage of the total time each individual will commit to the Program. This includes staff of the offeror and all proposed subcontractors.

SECTION 6: PROJECT MANAGEMENT

A. Provide a plan for the Program's organization, staffing, and management, including a detailed description of the role descriptions and level of effort of all proposed key scientific and technical personnel of the offeror and all proposed subcontractors and consultants. Provide an administrative framework indicating clear lines of authority and responsibility for all proposed Systems Biology Program personnel. Include a plan to manage, coordinate, and oversee the work performed by consultants and/or subcontractor(s). Include a chart of the

proposed organizational/management structure for the Program and each research Project.

B. Provide a detailed outline of the proposed milestones and associated timelines which shall be commensurate with the Technical Requirements of the BAA and the offeror's proposed Statement of Work.

C. Describe how the PI and PM will oversee the Program and perform project management activities to ensure that the proposed milestones and deliverables are achieved within the set timelines and budget.

D. Provide a plan for how the PI and PM will communicate with the Project Officer and Contracting Officer. Describe how the PI and PM will communicate with, monitor, and manage the Program's multidisciplinary teams at all performance sites to facilitate and encourage coordination and cooperation.

E. Provide a plan to establish the Systems Biology Working Group (SBWG) and describe the ideal composition and expertise of its members to provide advice on the management and performance of the Systems Biology Programs. Do not identify the names of any individual proposed for SBWG membership nor contact any specific individual regarding service on the SBWG.

SECTION 7: FACILITIES, EQUIPMENT, SAFETY, INFORMATION TECHNOLOGY (IT) AND DATA MANAGEMENT

The Technical Proposal should document availability and adequacy of safe facilities, equipment, space and other resources necessary to carry out the offeror's proposed Statement of Work, including:

A. A description of facilities, equipment and other resources of the proposed high-throughput technology cores where the informatics, functional genomics and proteomics cores will be utilized throughout all the years of contract performance period, and where at least one of the metabolomics, glycomics and lipidomics cores shall be utilized from year 2 through the end of the contract period.

B. Location and features of facilities, including a detailed floor plan showing the location of the equipment and other resources dedicated to the project for the prime contractor and any proposed subcontractors. Include a description of any facility modifications that would be accomplished prior to initiation and during the performance of the contract.

C. Documentation regarding the ownership/lease of the facility that demonstrates availability for the period of performance of the contract.

D. Biosafety Level (BSL) 2 and 3 biocontainment facilities for conducting work in accordance with the guidelines: http://www.cdc.gov/od/ohs/biosfty/bmbl5/bmbl5toc.htm.

E. A thorough summary of safe practices and facilities that will be available to assure a safe working environment for all personnel handling or in contact with pathogenic microorganisms. Describe the plans and procedures to be utilized to ensure compliance with all Federal and NIH safety guidelines and regulations,

including: monitoring of personnel; receiving, handling, storing, shipping and tracking Select Agents; and conducting work with recombinant DNA molecules.

F. Plans for training staff to operate facilities in accordance with BSL 2 and 3 guidelines, and for working with pathogenic microorganisms and host cells in accordance with Federal and NIH safety guidelines and regulations.

G. Describe the data management system for the secure storage, quality control, integration, and overall management of all contract-generated data and experimental results, as well as the data retrieved from pubic sources for research purposes.

H. Describe the IT system architecture, software development environment and computational infrastructure that will support the modeling activities, algorithms and software applications development, data analysis and integration, data dissemination and other computational needs of the Projects of the proposed Systems Biology Program.

I. Describe the network infrastructure that will allow the Program investigators access to the computational and database resources and software applications, to facilitate data sharing and electronic communication exchange among the Program's laboratories and to support the data dissemination goals of the Systems Biology Program.

SECTION 7: OTHER CONSIDERATIONS

Section L of the BAA provides minimum documentation requirements for the following items. The required information described in Section L should be assembled together, in the following clearly marked sections of the Technical Proposal. Refer to Section L of the BAA for specific requirements. Read each section below carefully. In some cases, offerors may be asked to provide documentation which is in addition to the minimum requirements identified in Section L.

a) Biological Agents or Toxins

The Technical Proposal should include a plan for biohazard safety and security requirements.

b) Obtaining and Disseminating Biomedical Research Resources

Section L of the BAA specifies the minimum documentation requirements for this element. The Technical Proposal should document all information necessary to evaluate this issue.

c) Sharing Research Data (Plan)

Section L of the BAA specifies the minimum documentation requirements for Data Sharing. All related documentation should be included in the proposal in this clearly marked section. The Technical Proposal should include a plan for Data Sharing as required by this BAA.

d) Information Technology (IT) Systems Security

Section L of the BAA specifies the minimum documentation requirements for IT Systems security. All related documentation should be included in the Technical Proposal in this clearly marked section. The Technical Proposal should include a plan for IT Systems security as required by this BAA.